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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/847,538	05/03/2001	Brita Schulze	062587-5002	4013

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EXAMINER	
SOROUSH, LAYLA	
ART UNIT	PAPER NUMBER
1617	
MAIL DATE	DELIVERY MODE
04/15/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/847,538	SCHULZE ET AL.	
	Examiner	Art Unit	
	LAYLA SOROUSH	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *58-60,63,65,67,69,74-77 and 79-82* is/are pending in the application.

4a) Of the above claim(s) *33,53-57,61,62,64,66,68,70-73 and 78* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *58-60,63,65,67,69,74-77 and 79-82* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 30, 2009. Claims 33, 53-82 are pending.

The following rejections are made:

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 58, 60, 63, 65, 67, 69, 75, 77, and 79-81 are rejected under 35 U.S.C. 102(b) as being anticipated by Kress et al. (WO 96/04017A1 (English Equivalent US Pat No. 6,048,515 – previously presented)).

Kress et al. teaches nanoparticles characterized in that they have an iron-containing core of iron or iron ions, a primary coat (synthetic polymer) and a secondary coat (target polymer), and optional auxiliary pharmaceutical substances, pharmaceuticals and/or adsorption mediators (Abstract; col 5 lines 45-46). The particles are useful as vehicles for medical substances in the field of therapeutics. The

specificity of the nanoparticles is used for the transport of medical substances to their place of action. The medical substances may be incorporated in the iron-containing core or chemically bonded to the synthesis polymer and/or the targeting polymer (col 17 lines 41-47). Such medical substances are inclusive of cytostatic agents (col 18, lines 13-15) and hormones. "As the nanoparticles combine high physical quality with excellent targetability by flexible adjustment (modular design) of the targeting polymer (secondary coat) to the respective problem, they are applicable for many special indications such as MR lymphography after intravenous or local interstitial administration, tumor visualization, visualization of functions or malfunctions, of plaque (atherosclerosis imaging), thrombi and vascular occlusions, MR angiography, perfusion imaging, infarct visualization, visualization of endothelial damages, receptor imaging, visualization of blood-brain barrier integrity etc., as well as for differential diagnosis, in particular, for distinguishing tumors/metastases from hyperplastic tissue (col 16 line 49-60)." "The nanoparticles according to the invention are further characterized in that they are available in the form of stable colloidal sols, which is preferred (col 5, lines 34-36)." "The hydrodynamic diameter of said basic structural unit (iron-containing core plus primary coat) in solution is smaller than 100 nm, preferably smaller than 50 nm, and not more than five times the diameter of the iron-containing core (col 5, lines 29-33)." "It is one of the specific advantages of the production method according to the invention that it offers great flexibility in the selection of synthesis polymers; the term "polymer" is not to be taken literally, as both low-molecular weight substances and mixtures of low- and polymolecular weight substances can be used for producing iron-containing cores.

Particularly preferred is the use of low-molecular and polymolecular substances that contain negative charge carriers in their molecule (col 12 lines 1-10)." "Low-molecular weight substances such as carboxypolyalcohols, polycarboxypolyalcohols, polycarboxyalcohols, carboxyalcohols, alcohols, monosugars, oligosugars, and synthesis polymers such as polyethylene glycol, polypropylene glycol and mixtures (block and copolymers), polyacrylic acid, polyvinyl alcohol, polylactic acid (polylactide and polylactide glycide), and natural or, specifically, partially synthetic or chemically and/or enzymatically modified natural polymers such as dextrans and its derivatives, arabinic acid, glycosaminoglycan and synthetic analogues, starch and its derivatives as well as gelatin derivatives. It is particularly preferable to use low-molecular weight derivatives of dextran that contain negative charge carriers(col 12 lines 23-40)."

Applicant is informed that a prior art composition that comprise all elemental components of the instantly created composition would meet all functional characteristics of the created composition, because such characteristics are inseparable from the composition. Kress et al. meets all elemental steps of the instant claims and the compositions created thereof. Since Kress et al.'s compositions are prepared by the same steps as the instantly claimed process and further comprise all elemental components of the instantly prepared composition, they would inherently exhibit the same zeta potentials, isoelectric point, and targeting properties as those instantly claimed, because such functional characteristics of the created composition is inseparable from the describe composition of Kress et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 59, 74, 76 and 82 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kress et al. (WO 96/04017A1 (English Equivalent US Pat No. 6,048,515– previously presented)) as applied to claim 58, 60, 63, 65, 67, 69, 75, 77, and 79-81 above, and further in view of Boehm et al. (J Pharm Belg. 2000 Mar-Apr;55(2)– previously presented).

Kress et al. is as discussed above.

Kress et al. fails to teach measuring the zeta potential of the composition or measuring the isoelectric point of the composition comprising the emulsions.

Boehm et al. teaches "Colloidal drug carriers which mainly involve submicron emulsions, nanoparticles, microparticles, liposomes and lipid complexes have received increasing interest in recent years mainly as vehicles of lipophilic drugs and as improved delivery systems for drug targeting. Size and encapsulation efficiency are, in general, the two parameters used to characterize these pharmaceutical forms. Nevertheless, the surface characteristics of these dispersion have been known to influence their physical, chemical and biological properties. Then, the aim of these study is to evaluate, with some examples and illustrations, the interest of zeta potential

determinations to improve the characterization of these colloidal drug carriers (abstract)."

Hence, one of ordinary skill in the art at the time of the invention when dealing with colloidal drug carriers would determine the zeta potential of the composition in order to determine surface characteristics of the dispersion for improving the colloidal drug carrier. The motivation is because one would have had a reasonable expectation of success in achieving the safest clinical outcome.

Additionally, since the "cationic agents" by definition must have a isoelectric point above 7 (see instant specification, pg. 15, at para 0057), absent a showing of unexpected results, it would have been obvious to one of ordinary skill in the art at the time of invention to optimize such parameters during the processes described by either Kress et al. by routine experimentations. The ordinary skill in the art would have been motivated to do such optimization to improve stability and delivery of such systems.

Response to Arguments

Applicant's arguments filed April January 30, 2009 have been fully considered.

Applicant's argument regarding the elected species is persuasive. Hence, claims 59, 74, 76, and 82 are incorporated in the rejection above.

Applicant argues the reference fails to teach cationic particles. Examiner states that the reference clearly teaches iron and iron ion particles which reads on a cationic particle.

Applicant argues the Kresse reference does not teach enhancing efficacy of an active agent to produce a composition having an optimal potential at a targeted a

vascular site. Examiner respectfully reiterates: Applicant is informed that a prior art composition that comprise all elemental components of the instantly created composition would meet all functional characteristics of the created composition, because such characteristics are inseparable from the composition. The references meet all elemental steps of the instant claims and the compositions created thereof. Since reference's compositions are prepared by the same steps as the instantly claimed process and further comprise all elemental components of the instantly prepared composition, they would inherently exhibit the same zeta potentials and targeting properties as those instantly claimed, because such functional characteristics of the created composition is inseparable from the describe composition of the references.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, one of ordinary skill in the art at the time of the invention when dealing with colloidal drug carriers would determine the zeta potential of the composition in order to determine surface characteristics of the dispersion for improving the colloidal drug carrier. The motivation is because one would have had a reasonable expectation of success in achieving the safest clinical outcome.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Layla Soroush whose telephone number is (571)272-5008. The examiner can normally be reached on Monday through Friday from 8:30 a.m. to 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1617